UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,785	03/14/2007	Werner Seeger	VJP-1050-US	4411

35938 7590 02/15/2011

BioTechnology Law Group
12707 High Bluff Drive
Suite 200
San Diego, CA 92130-2037

EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
02/15/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DOCKETING@BIOTECHNOLOGYLAWGROUP.COM

Office Action Summary	Application No.	Applicant(s)	
	10/583,785	SEEGER ET AL.	
	Examiner	Art Unit	
	CHIH-MIN KAM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-8,10-23 and 27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *16 and 17* is/are allowed.

6)☒ Claim(s) *1-3,6-8,10,11,14,15,18-23 and 27-34* is/are rejected.

7)☒ Claim(s) *12 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/2/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-3, 6-8, 10-23 and 27-34 are pending.

Applicants' amendment and declaration of Dr. Clemens Ruppert filed December 2, 2010 are acknowledged. Applicant's response and declaration of Dr. Clemens Ruppert have been fully considered. Claims 1, 6, 16, 17, 22 and 32 have been amended, and claims 4, 5 and 9 have been cancelled. Therefore, claims 1-3, 6-8, 10-23 and 27-34 are examined.

2. A proposed Examiner's amendment was faxed to the applicant on February 2, 2010, however, this amendment has not been accepted.

Withdrawn Informalities

3. The previous objection to the specification regarding the continuation data and nucleotide sequences cited at pages 7-8 is withdrawn in view of applicants' amendment to the specification and applicants' response at page 9 in the amendment filed December 2, 2010.

Withdrawn Claim Objections

4. The previous objection to claims 5, 10, 12 and 13 is withdrawn in view of applicants' amendment to the claim, and applicants' cancellation of the claims in the amendment filed December 2, 2010.

Withdrawn Claim Rejections - 35 USC § 101

5. The previous rejection of claims 16-17 under 35 U.S.C. 101 is withdrawn in view of applicants' amendment to the claim, and applicants' response at pages 10 in the amendment filed December 2, 2010.

Withdrawn Claim Rejections - 35 USC § 112

6. The previous rejection of claims 4 and 9 under 35 U.S.C. 112, first paragraph, scope of enablement, is withdrawn in view of applicants' cancellation of the claims in the amendment filed December 2, 2010.

7. The previous rejection of claims 22 and 32 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicants' amendment to the claim, and applicants' response at page 13 in the amendment filed December 2, 2010.

Claim Objections

8. Claim 15 is objected to because of the use of the term "encoding a fusion protein of claim 1". Since claim 15 is dependent from claim 1, it should use the term "encoding the fusion protein of claim 1". The same type of objection is also applied to claims 21, 22, 23, 27, 33 and 34. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3, 6-8, 10, 11, 14, 15, 18-23 and 27-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fusion protein comprising a specific mammalian surfactant protein precursor (e.g., SP-B) lacking its C-terminal propeptide fused at its C-terminus to the N-terminus of a plasminogen activator or comprising a mature surfactant protein N-terminally or C-terminally fused to a plasminogen activator, wherein the

surfactant protein is surfactant protein B (SP-B) or SP-C, wherein the fusion protein retains the biophysical property of the surface protein and the fibrinolytic activity of the plasminogen activator; a pharmaceutical composition comprising the fusion protein; a nucleic acid molecule comprising a nucleotide encoding the fusion protein; a vector or host cell comprising the nucleic acid molecule; a method for producing the fusion protein by expressing the nucleic acid molecule; and a method of treating an inflammatory and interstitial lung disease by administering the fusion protein, does not reasonably provide enablement for a fusion protein comprising a mammalian surfactant protein precursor (i.e., SP-B precursor) lacking its C-terminal propeptide fused at its C-terminus to the N-terminus of a plasminogen activator or comprising a mature surfactant protein N-terminally or C-terminally fused to a plasminogen activator, where the surfactant protein is SP-B or SP-C, but the structure and/or function of the fusion protein is not defined; a pharmaceutical composition comprising the fusion protein; a nucleic acid molecule comprising a nucleotide encoding the fusion protein; a vector or host cell comprising the nucleic acid molecule; a method for producing the fusion protein by expressing the nucleic acid molecule; and a method of preventing or treating an inflammatory and interstitial lung disease by administering the fusion protein. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-3, 6-8, 10, 11, 14, 15, 18-23 and 27-34 are directed to a fusion protein comprising a mammalian surfactant protein precursor (i.e., SP-B precursor) lacking its C-terminal propeptide fused at its C-terminus to the N-terminus of a plasminogen activator or comprising a mature surfactant protein (i.e., SP-B or SP-C) N-terminally or C-terminally fused to

a plasminogen activator; a nucleic acid molecule comprising a nucleotide encoding the fusion protein; a vector or host cell comprising the nucleic acid molecule; a method for producing the fusion protein by expressing the nucleic acid molecule; and a method of preventing or treating an inflammatory and interstitial lung disease by administering the fusion protein. The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the present invention relates to a fusion protein comprising a mammalian surfactant protein precursor lacking its C-terminal propeptide fused at its C-terminus to the N-terminus of a plasminogen activator or comprising a mature surfactant protein N-terminally or C-terminally fused to a plasminogen activator (page 5). There are no indicia that the present application enables the full scope in view of the claimed fusion protein and its method of making and using the fusion protein as discussed in the stated rejection. The present application does not provide sufficient teachings to enable the full scope of the claims. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the surfactant proteins and plasminogen activators in the fusion proteins, and the methods of preventing or treating inflammatory and interstitial lung diseases using the fusion proteins, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The specification shows that cloning of SPUC1A cDNA; expression of SPUC1A in CHO cells, and functional analysis of SPUC1A using chromogenic substrates or fibrin gel autography (Examples 1-4), where SPUC1A is a fusion protein of SP-$B_{\Delta C}$ N-terminally fused to LMW-u-PA. However, the specification does not show fusion proteins with various structures of surfactant proteins and plasminogen activators that are functional, and the use of various functional fusion proteins in preventing or treating inflammatory and interstitial lung diseases.

(3). The state of the prior art and relative skill of those in the art:

The related art (e.g., Rupport et al., Thrombosis and Hemostasis 89, 53-64 (2003)) discloses a hybrid molecule is obtained by chemical cross-linking of the mature surfactant protein SP-B and B chain of urokinase plasminogen activator, where the hybrid molecule retains the biophysical activity as compared to native SP-B, is about 2-3 fold more effective in lysis of surfactant-containing fibrin clots and is about 3-5 fold more resistant toward PAI-1 than native u-PA, thus resulting in chimeric enzymes with enhanced substrate specificity (page 3, lines 20-31 of the specification). However, the art does not teach the use or make of functional fusion proteins comprising various SP-B or SP-C with various plasminogen activators. Thus, the specification needs to provide specific guidance on the use or making of functional fusion proteins comprising various plasminogen activators and various SP-B or SP-C, to be considered enabling for the claimed method associated with the variants. Furthermore, regarding prevention of a lung disease, if the disease does not occur, it is not clear how to monitor the disease. Thus, the specification does not provide sufficient teachings in the prevention of inflammatory and interstitial lung diseases using the fusion protein.

(4). Predictability or unpredictability of the art:

The claims are directed to fusion proteins comprising a SP-B precursor fused to a plasminogen activator or comprising a mature SP-B or SP-C fused to a plasminogen activator; and a method of preventing or treating an inflammatory and interstitial lung disease by administering the fusion protein. While the specification shows the make and functional analysis of SPUC1A (i.e., a fusion protein of SP-$B_{\Delta C}$ N-terminally fused to LMW-u-PA), the specification does not demonstrate the use/make of functional fusion proteins comprising various plasminogen activators and various SP-B or SP-C, thus the effect of a fusion protein containing a different SP-B or SP-C and a different plasminogen activator in the treatment of inflammatory lung disease is unpredictable.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to fusion proteins comprising a SP-B precursor fused to a plasminogen activator or comprising a mature SP-B or SP-C fused to a plasminogen activator; and a method of preventing or treating an inflammatory and interstitial lung disease by administering the fusion protein. While the specification discloses the make and functional analysis of SPUC1A (i.e., a fusion protein of SP-$B_{\Delta C}$ N-terminally fused to LMW-u-PA; Examples 1-4) and the fusion protein retains the biophysical property of the surface protein and the fibrinolytic activity of the plasminogen activator (page 5, line 17-page 6, line 7), it does not discloses the use/make of functional fusion proteins comprising various plasminogen activators and various SP-B or SP-C. Thus, the effect of a fusion protein containing a SP-B or SP-C and a plasminogen activator in the treatment of an inflammatory lung disease is not predictable. Since

the specification does not provide sufficient teachings on the identification of a functional fusion protein comprising a plasminogen activator and a SP-B or SP-C, it is necessary to carry out undue experimentation to identify a fusion protein that is effective in treating an inflammatory and interstitial lung disease.

(6). Nature of the Invention

The scope of the claims encompasses a method of preventing or treating an inflammatory and interstitial lung disease by administering a fusion protein comprising a SP-B precursor or a mature SP-B or SP-C fused to a plasminogen activator, but the specification does not provide the sufficient teachings on the identification of a functional fusion protein that is effective in the treatment. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed variants and associated methods, the effects of fusion proteins in treating various inflammatory lung diseases are unpredictable, and the teachings in the specification are limited, therefore, it is necessary to carry out undue experimentation to identify a fusion protein that is effective in treating an inflammatory and interstitial lung disease.

Response to Arguments

Applicants indicate claim 1 has been amended to incorporate the limitations of dependent claim 5, which is indicated by the Examiner meets the enablement standard. Claim 6 has also been amended to provide the mature surfactant protein is SP-B or SP-C. Applicants submit that one of skill in the art would also acknowledge that the specification is enabling with regard to similar constructs in which SP-B is replaced with SP-C. In this regard, Applicants submit the declaration of Dr. Clemens Ruppert, which addresses the merits of the rejection (see below).

In the declaration of Dr. Clemens Ruppert, paragraph 5 states that SP-B and SP-C share certain structural characteristics such that SP-B and SP-C are both hydrophobic; each of SP-B and SP-C are synthesized as propeptides by type II alveolar cells, and both are processed to the mature hydrophobic peptide. The present specification teaches that a fusion partner can also act as the necessary shield for SP-B and SP-C as the "propeptide" portion of the SP-B and SP-C precursor acting as the "shield" in the natural environment; paragraph 6 states that Lucovic et al. (Biochem. Biophys. Acta 2006, 1758(4):509-518) confirms the teachings of the present invention regarding these shared properties of SP-B and SP-C; paragraph 7 states that the skilled artisan is also aware that SP-B and SP-C not only share structural characteristics, but also share functional characteristics, particularly in the context of lung injury and inflammation (e.g., Markart et al., Am J. Physiol. Lung Cell Mol. Physiol. 284:L69-L76 (2003)); and paragraph 8 states that one of skill in the art could readily extrapolate the working examples involving SP-B to SP-C in view of the well known similarities in structure and function between SP-B and SP-C. Thus, the claimed invention can be practiced throughout its scope with reference to the specification using no more than conventional techniques.

In conclusion, the claimed invention can be practiced throughout its scope without undue experimentation because the person of ordinary skill with reference to the specification understands its application and need use no more than conventional techniques to apply it. In view of the foregoing, applicants request the rejection be withdrawn (pages 10-13 of the response).

Applicants' response has been considered. Regarding SP-C, applicants' arguments are found persuasive. However, the amended claim 1 or 6 is directed to a fusion protein comprising

a SP-B precursor fused to a plasminogen activator or comprising a mature surfactant protein SP-B or SP-C fused to a plasminogen activator, where the structure and/or function of the fusion protein is not defined. Thus, the claims would encompass numerous fusion proteins with various structures of plasminogen activators and Sp-B or Sp-C, where the fusion protein can be either functional or non-functional. Other than SPUC1A, which is a fusion protein of SP-$B_{\Delta C}$ N-terminally fused to LMW-u-PA, the specification has not provided sufficient teachings to identify a functional fusion protein that is effective in treating an inflammatory and interstitial lung disease. Furthermore, applicants did not address the issue regarding how to use the fusion protein in the prevention of inflammatory and interstitial lung diseases. In view of the foregoing, claims 1-3, 6-8, 10, 11, 14, 15, 18-23 and 27-34 are rejected under 35 U.S.C. 112, first paragraph.

New Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 2, 3, 7, 8, 22 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 2 and 7 recites the limitation "one of the protein components (a) or (b)" in line 1. There is insufficient antecedent basis for this limitation in the claim.

12. Claims 3 and 8 recite the limitation "both protein components (a) and (b)" in line 1. There is insufficient antecedent basis for this limitation in the claim.

13. Claims 22 and 32 recites the limitation "obtained in (a)" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Objections

14. Claims 12 and 13 are objected to because the claims are dependent from a rejected claim.

Conclusion

15. Claims 1-3, 6-8, 10, 11, 14-15, 18-23 and 27-34 are rejected; and claims 12 and 13 are objected to. It appears that claims 16 and 17 are free of art and allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached at 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Chih-Min Kam/
Primary Examiner, Art Unit 1656

CMK
February 9, 2011